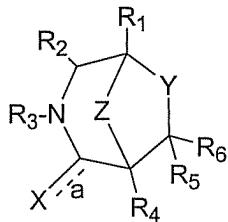


AMENDMENTS TO THE CLAIMS

1-21. (Cancelled)

22. (Currently Amended) A pharmaceutical composition comprising as active principle at least one among the 3-aza-bicyclo[3.2.1]octane derivatives of general formula (I), or mixtures thereof



I

wherein:

R₁ is H,

R₂ is selected from the group consisting of H, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, cycloalkyl, aryl, arylC₁₋₈alkyl, heterocycleC₁₋₈alkyl, aminoC₁₋₈alkyl, aminoaryl, C₁₋₈alkyloxyaryl, hydroxyaryl, hydroxyC₁₋₈alkyl, carboxyC₁₋₈alkyl, methyloxycarbonylC₁₋₈alkyl, carboxyaryl, carboalkyloxyaryl, alkylcarbamoylaryl and -(side chains of amino acids), or

R₃ is selected from the group consisting of H, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, cycloalkyl, aryl, arylC₁₋₈alkyl, heterocycleC₁₋₈alkyl, RR'NC₁₋₈alkyl, RR'Naryl, RO-C₁₋₈alkyl, RO(O)C-C₁₋₈alkyl, R(O)C-C₁₋₈alkyl, RC(O)O-C₁₋₈alkyl, RC(O)N(R)C₁₋₈alkyl, RO-aryl, RO(O)C-aryl, R(O)C-aryl RC(O)O-aryl, RC(O)N(R)aryl, -CH(amino acid side-chain)CO₂R, -CH(amino acid side-chain)C(O)NR, -CH(CO₂R)- amino acid side-chain, CH(CONRR')- amino acid side-chain, Fmoc, Boc and Cbz,

R₄, and R₅, equal or different amongst each other, are selected from the group consisting of H, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, cycloalkyl, aryl, heterocycle, arylC₁₋₈alkyl and heterocycleC₁₋₈alkyl,

R₆ is selected from the group consisting of H, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, cycloalkyl, aryl, arylC₁₋₈alkyl, heterocycle, heterocycleC₁₋₈alkyl; -C(O)R, -C(O)OR, -C(O)NRR', CH₂OR, CH₂NRR', -C(O)NH-CH(amino acid side-chain)C(O)OR, CH₂NR-Fmoc, CH₂NR-Boc and CH₂NR-CBz,

R and R', equal or different between each other, are selected from the group consisting of H, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, cycloalkyl, aryl, heterocycle, arylC₁₋₈alkyl; heterocycleC₁₋₈alkyl; protecting group, -C(O)CH-(amino acid side-chain)-NHT, -NH-CH(amino acid side-chain)COOT and -CH(amino acid side-chain)COOT,

where T is selected from between H and C₁₋₈alkyl;

X is O, α is a double bond,

Y and Z, equal or different from each other, are selected from the group consisting of O, S, SO, SO₂ and N-R, wherein R is as above defined;

Q is selected from the group consisting of C=O, CH₂, CO-NH-CH (amino acid side-chain)-CO, CONR(CH₂)_nCO, CONR-C₂₋₈alkenyl-CO C(O)O(CH₂)_nCO, CH₂OC(O)(CH₂)_nCO, and

CH₂NRC(O)(CH₂)_nCO, wherein n is comprised between 2 and 6, and R is as above defined,

Q' is selected from the group consisting of C(O)OCH₂, C(O)NRCH₂, CH₂OC(O), CH₂NRC(O),

CONR(CH₂)_nNRCO, CONR-C₂₋₈alkenyl-NRCO, C(O)O(CH₂)_nNRCO, CONR(CH₂)_nOC(O),

CH₂OC(O)(CH₂)_nOC(O)CH₂, CH₂NRC(O)(CH₂)_nNRC(O)CH₂, CH₂OC(O)(CH₂)_nNRC(O)CH₂,

CH₂NRC(O)(CH₂)_nOC(O)CH₂, CH₂NR(CH₂)_nNRCH₂, CH₂O(CH₂)_nOCH₂, CH₂O(CH₂)_nNRCH₂,

and CH₂NR(CH₂)_nOCH₂, wherein n is comprised between 2 and 6, and R is as above defined,

and where the groups alkyl, alkenyl, alkynyl, cycloalkyl, aryl and the heterocyclic groups above reported, are possibly substituted; and

a pharmaceutically acceptable excipient or diluent

~~wherein said pharmaceutical composition is for use in the treatment of diseases in which neurotrophine functions are involved in defect.~~

23. (Previously Presented) The pharmaceutical composition according to claim 22, wherein Z is O.

24. (Previously Presented) The pharmaceutical composition according to claim 22, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, aryl and heterocyclic groups may be substituted with one or more moieties chosen from the group consisting of halogen, cyano, nitro, amino, hydroxy, carboxylic acid, carbonyl and C₁₋₆alkyl.

25. (Previously Presented) The pharmaceutical composition according to claim 22, wherein the 3-aza-bicyclo[3.2.1]octane derivatives of formula (I) are selected from the compounds having the following formulas:

Compound	X	R ₁	R ₂	R ₃	R ₆
1	O	H	H	PhCH ₂	(R) -CO ₂ Me
2	O	H	H	PhCH ₂	(S) -CO ₂ Me
3	O	H	H	PhCH ₂	(R)-CONCyclohexyl
4	O	H	H	PhCH ₂	(R)-CONCyclopentyl
5	O	H	(S) -Me	PhCH ₂	(R) -CO ₂ Me
6	O	H	(S) -Me	PhCH ₂	(S) -CO ₂ Me
7	O	H	(R) -Me	PhCH ₂	(R) -CO ₂ Me
8	O	H	(R) -Me	PhCH ₂	(S) -CO ₂ Me
9	O	H	(R) -CH ₂ Ph	PhCH ₂	(S) -CO ₂ Me
10	O	H	(R) -CH ₂ Ph	PhCH ₂	(R) -CO ₂ Me
11	O	H	(S) -CH ₂ Ph	PhCH ₂	(S) -CO ₂ Me
12	O	H	(S) -CH ₂ Ph	PhCH ₂	(R) -CO ₂ Me
13	O	H	(S)-CH ₂ OBn	PhCH ₂	(R) -CO ₂ Me
14	O	H	(S)-CH ₂ OBn	PhCH ₂	(S) -CO ₂ Me
15	O	H	(R)-CH ₂ OBn	PhCH ₂	(R) -CO ₂ Me

16	O	H	(R)-CH ₂ OBn	PhCH ₂	(S)-CO ₂ Me
17	O	H	(S)-CH ₂ OH	PhCH ₂	(R)-CO ₂ Me
18	O	H	(S)-CH ₂ OH	PhCH ₂	(S)-CO ₂ Me
19	O	H	(R)-CH ₂ OH	PhCH ₂	(R)-CO ₂ Me
20	O	H	(R)-CH ₂ OH	PhCH ₂	(S)-CO ₂ Me
21	O	H	=CH ₂	PhCH ₂	(R)-CO ₂ Me
22	O	H	=CH ₂	PhCH ₂	(S)-CO ₂ Me
23	O	H	(R)-CH ₂ OH	PhCH ₂	(S)-CO ₂ Me

Compound	X	R ₁	R ₂	R ₃	R ₆	(I)						
190	O	H	H	PhCH ₂	(R)-CO ₂ Me							
191	O	H	H	PhCH ₂	(S)-CO ₂ Me							
192	O	H	(S)-Me	PhCH ₂	(R)-CO ₂ Me							
193	O	H	(S)-Me	PhCH ₂	(S)-CO ₂ Me							
194	O	H	(R)-Me	PhCH ₂	(R)-CO ₂ Me							
195	O	H	(R)-Me	PhCH ₂	(S)-CO ₂ Me							
196	O	H	(S)-PhCH ₂	PhCH ₂	(R)-CO ₂ Me							
197	O	H	(S)-PhCH ₂	PhCH ₂	(S)-CO ₂ Me							
198	O	H	(R)-PhCH ₂	PhCH ₂	(R)-CO ₂ Me							
199	O	H	(R)-PhCH ₂	PhCH ₂	(S)-CO ₂ Me							
200	O	H	(S)-CH ₂ CH(Me) ₂	PhCH ₂	(R)-CO ₂ Me							
201	O	H	(S)-CH ₂ CH(Me) ₂	PhCH ₂	(S)-CO ₂ Me							
202	O	H	(R)-CH ₂ CH(Me) ₂	PhCH ₂	(R)-CO ₂ Me							
203	O	H	(R)-CH ₂ CH(Me) ₂	PhCH ₂	(S)-CO ₂ Me							
204	O	H	H	PhCH ₂	(R)-CONHMe							

205	O	H	H	PhCH ₂	(S) -CONHMe
206	O	H	(S) -Me	PhCH ₂	(R) -CONHMe
207	O	H	(S) -Me	PhCH ₂	(S) -CONHMe
208	O	H	(R) -Me	PhCH ₂	(R) -CONHMe
209	O	H	(R) -Me	PhCH ₂	(S) -CONHMe
210	O	H	(S) -PhCH ₂	PhCH ₂	(R) -CONHMe
211	O	H	(S) -PhCH ₂	PhCH ₂	(S) -CONHMe
212	O	H	(R) -PhCH ₂	PhCH ₂	(R) -CONHMe
213	O	H	(R) -PhCH ₂	PhCH ₂	(S) -CONHMe
214	O	H	(S) -CH ₂ CH(Me) ₂	PhCH ₂	(R) -CONHMe
215	O	H	(S) -CH ₂ CH(Me) ₂	PhCH ₂	(S) -CONHMe
216	O	H	(R) -CH ₂ CH(Me) ₂	PhCH ₂	(R) -CONHMe
217	O	H	(R) -CH ₂ CH(Me) ₂	PhCH ₂	(S) -CONHMe

26. (Cancelled)

27. (Withdrawn) A method of treating:

- i) neurodegenerative, inflammatory, toxic, traumatic, or vascular disorders of the central, peripheral, or autonomic nervous system, neural damages secondary to hypoxia, ischaemia, burns, chemotherapy, toxic compounds of various origin (including alcohol), infections, trauma (including surgical trauma) originating axotomy of motoneurons, sensorial, motor, or sensorimotor neuropathies, or autonomic dysfunctions secondary to diverse pathologies, genetic disorders, nervous pathologies of diverse origin, some ocular pathologies, corneal diseases of diverse origin, pathologies from reduced motility of the gastro-intestinal tract or from urinary bladder atony, endocrine neoplastic pathologies, clinical conditions in which stimulation of learning processes is advantageous, and all pathological conditions originating from apoptotic processes of neural cells;
- ii) acquired immunodeficiency diseases due to reduced or absent bioavailability of NGF;
- iii) conditions in which stimulation of neoangiogenesis may be advantageous;
- iv) certain ocular pathologies,

said method comprising administering to a patient in need of such a treatment a pharmaceutical composition comprising as active principle at least one among the 3-aza-bicyclo[3.2.1]octane derivatives of general formula (I), or their dimers of general formula (II) and (III), or mixtures thereof as defined in claim 22.

28. (Withdrawn) The method according to claim 27, in which said neurodegenerative, inflammatory, toxic, traumatic, or vascular disorders of the central, peripheral, or autonomic nervous system are selected from Alzheimer Disease (AD), Amyotrophic Lateral Sclerosis (ALS), Huntington disease, multiple sclerosis, epilepsy, Down syndrome, nervous deafness and Ménière's disease.

29. (Withdrawn) The method according to claim 27, in which said neural damages secondary to infections are selected from polio and HIV virus.

30. (Withdrawn) The method according to claim 27, in which said genetic disorders are selected from Charcot-Marie-Tooth disease, Refsum disease, abetalipoproteinemia, Tangier disease, Krabbe disease, metachromatic leukodystrophy, Fabry disease, Dejerine-Sottas disease.

31. (Withdrawn) The method according to claim 27, in which said nervous pathologies of diverse origin are selected from diffuse atrophy of cerebral cortex, Lewy body dementia, Pick's disease, mesolimbocortical dementia, neuronal ceroid lipofuscinosis, thalamic degeneration, cortico-striatal-spinal degeneration, cortico-basal ganglionic degeneration, cerebro-cerebellar degeneration, familial dementia with spastic paraparesis, polyglucosan bodies disease, Shy-Drager syndrome, olivopontocerebellar atrophy, progressive supranuclear palsy, deforming muscular dystony, Hallervorden-Spatz disease, Meige's syndrome, familial shivering, Gilles de la Tourette syndrome, chorea-acanthocytosis syndrome, Friedreich's ataxia, Holmes' corticocerebellar familial atrophy, Gerstmann-Straussler-Scheinker disease, progressive spinal muscular atrophy, spastic paraplegia, peroneal muscular atrophy, hypertrophic interstitial polyneuropathy and polyneuritic ataxic heredopathy.

32. (Withdrawn) The method according to claim 27, in which said ocular pathologies are selected from optic nerve neuropathies, retinal degeneration, ophtalmoplegy and glaucoma; and said corneal diseases of diverse origin are selected from neurotrophic ulcers, post-traumatic and post-infective corneal disorders.

33. (Withdrawn) The method according to claim 27, in which said pathologies from reduced motility of the gastro-intestinal tract or from urinary bladder atony are selected from interstitial cystitis and diabetic cystitis.

34. (Withdrawn) The method according to claim 27, in which said conditions in which stimulation of neoangiogenesis may be advantageous are selected from myocardial infarction, stroke, cerebral aneurysms, gastro-duodenal ulcers, wound healing and peripheral vasculopathies.

35. (Withdrawn) The method according to claim 27, in which said acquired immunodeficiency disease is immunodeficiency of ageing.

36. (Withdrawn) A method for promoting growth and/or *in vivo*, *in vitro* or *ex vivo* survival of neuronal cells, comprising using as promoting reagents the 3-aza-bicyclo[3.2.1]octane derivatives of formula (I), their dimers of formula (II) or (III) and mixtures thereof as defined in claim 22.

37. (Withdrawn) The method according to claim 36, wherein said neural cells are selected from the group consisting of dopaminergic, cholinergic, sensorial neurons, striatal cells, cortical cells, cells of the corpus striatum, hippocampus, cerebellum, olfactory bulbs, peri-aqueductal cells, cells of the raphe nuclei, of the locus coeruleus, of the dorsal root ganglia, sympathetic neurons, lower motoneurons, nervous stem cells, and cells anyhow deriving from the neural plaque.

38. (Withdrawn) A process for the preparation of culture and storage media useful for conservation of explanted corneas destined to transplantation, comprising adding to culture and

storage media 3-aza-bicyclo[3.2.1]octane derivatives of formula (I), their dimers of formula (II) or (III), or mixtures thereof as defined in claim 22.

39. (Withdrawn) A method for imaging analysis of tissues and organs containing neurotrophine receptors, comprising using 3-aza-bicyclo[3.2.1]octane derivatives of formula (I), their dimers of formula (II) or (III), or mixtures thereof as defined in claim 22, labelled with suitable reagents (contrast agents, radioisotopes, fluorescent agents etc.), and possibly processed with procedures useful for medical imaging purposes.

40. (Withdrawn) The method according to claim 39, for monitoring the use and efficacy of drugs or for the diagnosis of mammal diseases in which the neurotrophine receptors are involved.

41. (Cancelled)

42. (Currently Amended) The 3-aza-bicyclo[3.2.1]octane derivatives of formula (I) selected from the compounds indicated by the following numbers: 3,4,6,11,14-16,18,22-23,190-191, and 196-217, as defined in claim 25.